A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP4357.

The Usual (and Some Not-So-Usual) Suspects: A New Chemical Screening Method

Rachel Cernansky

https://doi.org/10.1289/EHP4357

With more than 40,000 active chemicals registered for use in the United States,[1] researchers cannot always easily determine the chemicals to which we are actually exposed. A recent report in *Environmental Health Perspectives* discusses a new method that may enable investigators to more efficiently screen biosamples for multiple chemicals at once.[2]

In developing and testing the method, the researchers also identified a number of chemicals in women's blood that had not been evaluated in previous targeted biomonitoring studies, including analyses of the National Health and Nutrition Examination Survey. This survey monitors levels of a few hundred preselected chemicals, but it is not designed to test for unknown substances.[3]

For the current study, the researchers began with a database of 696 organic compounds from a variety of chemical classes, as well as known or predicted metabolites of some environmental chemicals. Many of these chemicals are used in consumer products; several of them are known or suspected to have endocrine activity.

The researchers recruited 75 pregnant women who were receiving prenatal care at two San Francisco hospitals. They collected blood samples when the women gave birth. An initial nontargeted analysis using high-resolution mass spectrometry yielded evidence of highly detected "suspect peaks" or "suspect features" that had masses consistent with chemicals included in the database. The team then used successive data processing steps and *a priori* criteria to select a subset of suspect features for chemical confirmation.

Analysis revealed an average of 56 suspect features in the samples. The researchers focused on frequently identified suspect peaks that did not correspond to compounds measured in previous biomonitoring studies. Ultimately, they confirmed the presence of six chemicals that had not been evaluated in previous biomonitoring studies.

That confirmation is a significant accomplishment, says Frederica Perera, director of Columbia University's Center for Children's Environmental Health. "Data have been lacking on the full spectrum of environmental chemicals in the bodies of pregnant women," says Perera, who was not involved with the study. "This proof-of-principle study takes an important step in addressing this problem by demonstrating novel methods to screen for a wide range of potentially toxic chemicals."

Physiological changes during pregnancy mean that women's bodies may respond differently than when they are not pregnant to environmental exposures. However, little is known about the spectrum of exposures that pregnant women encounter. A new proof-of-principle study demonstrates a novel method for screening for a wide range of chemicals. Image: © Rawpixel Ltd/Alamy Stock Photo.

Developing capacity to do that kind of screening is crucial for studying the exposome, or the totality of exposures a person experiences.[4] Studying pregnant women is also particularly important in part because physiological changes during pregnancy (such as increased plasma and blood volume[5]) may affect the concentrations of chemicals in a woman's body.[6]

The approach falls short, however, because it is less sensitive than more targeted methods of screening for prespecified individual chemicals, such as traditional biomonitoring.[7] Nevertheless, the targeted methods are limited by the very fact that they search for a small set of substances at a time.

The authors note that their semitargeted approach and subsequent prioritization of suspect features for confirmation would not identify all environmental chemicals and metabolites to which the women were exposed. "We're probably picking up less than the full picture in terms of exposures," says Tracey Woodruff, director of the Program on Reproductive Health and the Environment at the University of California, San Francisco, and senior author of the study.

Gary Miller, vice dean for research strategy and innovation at the Columbia University Mailman School of Public Health, says that's a shortcoming in this study and in the field more broadly, because it keeps the research focused on known unknowns and limits the discovery of chemical features we do not yet know to look for. So much more information in the potential data set would exist if we loosened the validation standard, says Miller, who was not involved with the study. He adds, "I think we're doing ourselves a disservice to feel we have to validate these things to that level."

Miller argues that researchers doing exposure studies need to cast a wider net to find new clues about how the environment in all its complexity influences health. Casting a wider net probably means being less conservative in the level of precision they demand of themselves when determining the presence of chemicals, at least in the identification phase.

Otherwise, Miller says, too many suspects will be left behind. "There must be room for description of chemical features that may not have an authentic standard," he says. "For example, if a chemical is metabolized by your gut microbiome, that metabolite is very unlikely to have a standard. Thus, we ignore it even though it could be a key contributor to a health outcome."

Woodruff says the team is already working to scale up the method; they are scanning for 3,000 chemicals now, up from the nearly 700 covered by the current study. She acknowledges that six chemicals may not sound significant in comparison with the 40,000-plus out there. "This is really a crude first cut," she says. "We anticipate there'll be more. We just do not know how many more."

Rachel Cernansky is a freelance journalist in Denver, Colorado, covering science, health, and the environment. She has written for publications including *Nature*, *The Washington Post*, and *The New York Times*.

References

1. U.S. Environmental Protection Agency. 2019. EPA Releases First Major Update to Chemicals List in 40 Years. [Press Release.] 19 February 2019. https://www.epa.gov/newsreleases/epa-releases-first-major-update-chemicals-list-40-years [accessed 4 March 2019].
2. Wang A, Gerona RR, Schwartz JM, Lin T, Sirota M, Morello-Frosch R, et al. 2018. A suspect screening method for characterizing multiple chemical exposures among a demographically diverse population of pregnant women in San Francisco. Environ Health Perspect 126(7):077009, PMID: 30044231, https://doi.org/10.1289/EHP2920.
3. U.S. Centers for Disease Control and Prevention. 2019. *The Fourth National Report on Human Exposure to Environmental Chemicals*. Updated Tables, January 2019, Vol. One. Atlanta, GA:Centers for Disease Control and Prevention.
4. Wild CP. 2005. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol Biomarkers Prev 14(8):1847–1850, PMID: 16103423, https://doi.org/10.1158/1055-9965.EPI-05-0456.
5. Chesley LC. 1972. Plasma and red cell volumes during pregnancy. Am J Obstet Gynecol 112(3):440–450, PMID: 4551251, https://doi.org/10.1016/0002-9378(72)90493-0.
6. Woodruff TJ, Zota AR, Schwartz JM. 2011. Environmental chemicals in pregnant women in the United States: NHANES 2003–2004. Environ Health Perspect 119(6):878–885, PMID: 21233055, https://doi.org/10.1289/ehp.1002727.
7. Dennis KK, Marder E, Balshaw DM, Cui Y, Lynes MA, Patti GJ, et al. 2017. Biomonitoring in the era of the exposome. Environ Health Perspect 125(4):502–510, PMID: 27385067, https://doi.org/10.1289/EHP474.